REMARKS

This amendment is submitted in an earnest effort to bring this case to issue without delay.

Applicants appreciate the Examiner's indication that claims 9 and 12 are free of the prior art. However, Applicants believe that all of the claims now presented are free of the prior art.

Applicants have canceled claims 26 and 27 and added new claims 28 through 33. Antecedent basis for the new claims may be found in the specification on page 24, lines 1 to 12, page 30, lines 5ff, and in all of the following examples, for example see page 35, lines 5ff and 27ff, and page 36, lines 15ff. Thus claims 1 through 8, 10, 11, 13 through 25, and 28 through 33 are now in the application and are presented for examination.

Applicants have responded to the Examiner's rejection of claims 26 and 27 under 35 USC 112, first paragraph, as failing to comply with the enablement requirement, by canceling those claims and replacing those claims with new claims 28 through 33. New claims 28 through 33 recite a series of method steps as suggested by the Examiner at the top of page 4 of the office action. All of claims 28 through 33 include a contacting step, a detection step and a correlation step as suggested by the Examiner. Thus claims 28 through 33 fully comply with the enablement requirement of 35 USC 112, first paragraph.

The Examiner has found and applied a new reference, US Patent 5,093,258 to COHEN et al, and has combined the new reference with US Patent 5,744,141 to PAOLETTI et al and MEN et al to argue for the obviousness of all claims now presented except for claims 9 and 12. The Examiner relies on COHEN et al for its disclosure of a recombinant poxvirus that may include insertion of one or more foreign genes. The Examiner specifically refers to col. 3, lines 60 to 64 to show the preparation of the recombinant poxvirus and to col. 4, lines 44 to 46 and Figure 3 for the disclosure of the recombinant poxvirus. The Examiner indicates that it would be obvious to insert the two foreign genes disclosed in PAOLETTI et al at two different insertion sites as disclosed in COHEN et al, col. 4, lines 42 to 44. Thus the Examiner refuses to allow the remaining claims.

Applicants do not believe that the combination of PAOLETTI et al and COHEN et al would lead one skilled in the art to the present invention and so do not agree with the Examiner's conclusion that the present invention would be obvious to those skilled in the art. PAOLETTI et al does disclose the insertion of two or more homologous foreign genes into a poxvirus; however, those homologous foreign genes are inserted at the same insertion site, and not at different insertion sites as in the present invention. COHEN et al discloses the insertion of one or more foreign DNA sequences into a vector and carrying our homologous recombination of a fowlpox virus with that vector to obtain a recombinant fowlpoxvirus. See claim 6. COHEN et al also discloses

the insertion of foreign DNA into more than one insertion site as discussed hereinabove. However, COHEN et al does not disclose the insertion into a poxvirus of at least two foreign genes which are homologous in comparison to each other at two different insertion sites in the same poxvirus. There is no disclosure or suggestion in COHEN et al of inserting two homologous genes, such as those from Dengue Virus, into the same poxvirus.

The COHEN et al reference only generally discloses (or better only proposes) the insertion of foreign genes or "genes of interest" into a fowlpox genome, wherein "genes of interest" are broadly defined as "those which include immunogenic proteins of a pathogenic organism." See col. 5 of COHEN et al, second paragraph, first sentence. However, there is no recombinant disclosed in this document which encodes in its genome any "gene of interest" as defined. According to the examples, only marker genes have been inserted into the fowlpox genome. The whole disclosure in COHEN et al is focused on suitable promoters and vectors and on methods of how recombinants are obtained.

The combination of PAOLETTI et al and COHEN et al would not lead those skilled in the art to the present invention. Applicants maintain that they have discovered that these recombinant poxviruses prepared according to the present invention are surprisingly stable immunogens and are not subject to homologous recombination as would have been expected. See page 9 of the application where it is mentioned that the foreign homologous genes, inserted at remote sites into the poxviral

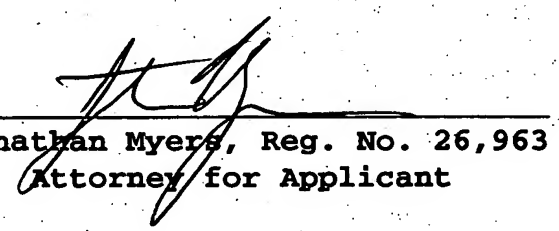
genome, would have been expected to be deleted. Homologous recombination would not be expected to be a problem if the two foreign homologous genes abut one another as in PAOLETTI et al. It is noted that the frequency of recombination is proportional to the distance between the linked genes, and so events between two or more homologous genes located in different sites as in the present invention would be expected to be high, and conversely events between two abutting homologous genes in PAOLETTI et al would be expected to be low. See page 10 of the present application. Thus the fact that PAOLETTI et al discloses insertion of two homologous genes into the same site of a viral vector in no way is suggestive of the presently claimed invention, notwithstanding that COHEN et al discloses the insertion of one or more foreign DNA sequences into a vector and carrying our homologous recombination of a fowlpox virus with that vector to obtain a recombinant fowlpoxvirus.

Nor does the fact that MEN et al discloses that MVA-BN is a well known safe viral vector that is especially suitable as a vector because it is a highly attenuated virus and cannot replicate in mammalian cells provide any basis in combination with PAOLETTI et al or COHEN et al to reject any claim now presented as obvious under 35 USC 103. Once again there is no suggestion in PAOLETTI et al, COHEN et al or MEN et al, where these references are taken individually or cumulatively of the insertion into a poxvirus of at least two foreign genes which are homologous in comparison to each other at two different insertion sites in the same poxvirus.

Furthermore this combination of references does not suggest that such insertion of two or more homologous foreign genes at two different insertion sites would result in a stable recombinant with no instability caused by homologous recombination between the inserted genes. Thus no rejection of any claim now presented as obvious under 35 USC 103 should be maintained.

Applicants believe that all claims now presented are in condition for allowance and a response to that effect is earnestly solicited.

Respectfully submitted,
The Firm of Karl F. Ross P.C.



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